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08/25/2006

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EXAMINER

STEADMAN, DAVID J

ART UNIT

PAPER NUMBER

1656

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PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/590,661	HAYASHI ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 25 February 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-16 is/are pending in the application.
- 4a) Of the above claim(s) 12-16 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-11 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 15 December 2006 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)            | 4) <input type="checkbox"/> Interview Summary (PTO-413)                   |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application         |
| Paper No(s)/Mail Date <u>8/25/06, 12/15/06</u> .                                       | 6) <input checked="" type="checkbox"/> Other: <u>Appendices A&amp;B</u> . |

## **DETAILED ACTION**

### ***Status of the Application***

**[1]** Claims 1-16 are pending in the application.

### ***Election/Restriction***

**[2]** Applicant's election with traverse of Group I, claims 1-11, in the reply filed on 2/25/08 is acknowledged. The traversal is on the ground(s) that claims 12-16 should be rejoined upon allowance of one or more of the elected claims. This is not found persuasive because the elected claims are not in a condition for allowance and thus consideration of claims 12-16 for rejoinder with the claims of elected Group I is not as yet required.

The requirement is still deemed proper and is therefore made FINAL.

**[3]** Claims 12-16 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 2/25/08.

### ***Information Disclosure Statement***

**[4]** All references cited in the information disclosure statements (IDSs) filed on 8/25/06 and 12/15/06 have been considered by the examiner. A copy of each Form PTO-1449 is attached to the instant Office action.

***Claim for Priority***

**[5]** This application is a 35 U.S.C. 371 national stage filing of PCT/JP05/03205, filed on 2/25/05, which claims foreign priority under 35 U.S.C. 119(a) to (d) to Japanese application 2004-049123, filed on 2/25/04. A certified copy of each of the Japanese priority document has been filed in the instant application on 8/25/06.

***Specification/Informalities***

**[6]** The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: ---Expression Vector Encoding a Triterpene Hydroxylase Polypeptide---.

***Claim Objection***

**[7]** Claim 1 is objected to and in order to substantially improve claim form, it is suggested that the claim be amended to more clearly identify each part of the claimed expression vector by, for example, reciting:

An expression vector having:

1) a polynucleotide: i) which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8 under a stringent condition and ii) encodes a polypeptide that has the activity of hydroxylating the 24-position of an oleanane type triterpene.

**[8]** Claim 6 is objected to and in order to substantially improve claim form, it is suggested that the claim be amended to more clearly identify each part of the claimed expression vector by, for example, reciting:

An expression vector having:

1) a polynucleotide: i) which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8 under a stringent condition and ii) encodes a polypeptide that has the activity of hydroxylating the 24-position of an oleanane type triterpene; and

2) a  $\beta$ -amyrin synthase gene.

***Claim Rejections - 35 USC § 112, Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

**[9]** Claims 1-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

**[a]** Claims 1 (claims 2-5 dependent therefrom) and 6 (claims 7-10 dependent therefrom) recite the limitation "a stringent condition". The claims are indefinite in the recitation of "a stringent condition" as the specification does not define with particularity what conditions constitute "stringent". What hybridization conditions are considered "stringent" varies widely in the art depending on the individual situation as well as the person making the determination. While it is acknowledged the specification discloses

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an “illustrative” example of a “stringent condition” (paragraph bridging pp. 9-10). However, this disclosure is non-limiting, providing only an exemplary “stringent” hybridization condition. As such it is unclear as to how identical to the sequence of SEQ ID NO:8 a sequence must be to be included within the scope of these claims. It is suggested that applicant clarify the meaning of the noted phrase.

**[b]** Claims 1 (claims 2-5 dependent therefrom) and 6 (claims 7-10 dependent therefrom) recite the limitation “polynucleotide represented by SEQ ID NO:8”. The claims are indefinite because it is unclear as to the intended meaning of the term “represented” with respect to SEQ ID NO:8. According to Webster’s online dictionary, a definition of “represent” is to serve as an example of (obtained from [www.merriam-webster.com/](http://www.merriam-webster.com/), last viewed on 4/2/08). As such, it is unclear as to whether applicant intends for “polynucleotide represented by SEQ ID NO:8” to be limited to SEQ ID NO:8, or whether SEQ ID NO:8 is merely an example. In the interest of advancing prosecution, the examiner has applied the broadest reasonable interpretation of the phrase as meaning SEQ ID NO:8 is merely an example. See MPEP 2111.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

**[10]** Claims 3 and 8 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. According to MPEP 2105, “If the broadest

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reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter". The claims are drawn to a transformant in which a host is transformed with an expression vector. According to the specification at p. 13, paragraph 13, "As examples of the host, a microorganism, a plant, an animal and the like can be cited, though not particularly limited". As such, the transformant of claims 3 and 8 encompasses an animal, *e.g.*, a human being, as the recited "host" and thus the claims encompass non-statutory subject matter.

***Claim Rejections - 35 USC § 112, First Paragraph***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

**[11]** Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

CLAIM INTERPRETATION: According to MPEP 2163.II.A.1, in evaluating a claimed invention for adequate written description, the examiner should determine what the claim as a whole covers. "Claim construction is an essential part of the examination

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process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997)."

The claims recite a genus of expression vectors having a polynucleotide which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8 under a stringent condition and also encodes a polypeptide that has the activity of hydroxylating the 24-position of an oleanane type triterpene, optionally further having a  $\beta$ -amyrin synthase gene. Regarding the phrase "a polynucleotide which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8", it is noted that: 1) "a complementary chain" has been interpreted as encompassing fragments of "the polynucleotide represented by SEQ ID NO:8" of as few as two contiguous nucleotides and 2) as noted above, the phrase "polynucleotide represented by SEQ ID NO:8" has been broadly but reasonably interpreted as meaning SEQ ID NO:8 is an example of such a polynucleotide. The phrase "the activity of hydroxylating the 24-position of an oleanane-type triterpene" has been interpreted as encompassing hydroxylating position 24 of any triterpene considered to be an "oleanane-type" triterpene. Also, regarding the phrase, " $\beta$ -amyrin synthase gene", it is noted that the phrase has been interpreted as meaning any nucleic acid that encodes a polypeptide having  $\beta$ -amyrin synthase activity and although the phrase recites "gene", the phrase has not been interpreted as being limited to those nucleic acids that are "naturally-occurring".



For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the specification discloses only a single representative species of the recited polynucleotides encoding a polypeptide that “has the activity of hydroxylating the 24-position of an oleanane type triterpene”, i.e., SEQ ID NO:8, which encodes a polypeptide that hydroxylates position 24 of  $\beta$ -amyrin and sophoradiol. Also, the specification discloses only a single representative species of the recited  $\beta$ -amyrin synthase gene, i.e., pea-derived  $\beta$ -amyrin synthase gene PSY (Morita et al., *Eur. J. Biochem.*, 267, 3543-3460, 2000). The specification fails to describe any additional representative species of the claimed genus. While MPEP § 2163 acknowledges that in certain situations “one species adequately supports a genus”, it is also acknowledges that “[f]or inventions in an unpredictable art, adequate written description of a genus

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which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of polynucleotides encoding a polypeptide that "has the activity of hydroxylating the 24-position of an oleanane type triterpene and  $\beta$ -amyrin synthase genes encompasses species that are widely variant with respect to structure. As such, it is the examiner's position that the disclosure of the single representative species of polynucleotides encoding a polypeptide that "has the activity of hydroxylating the 24-position of an oleanane type triterpene and  $\beta$ -amyrin synthase genes as noted above is insufficient to be representative of the attributes and features of *all* species encompassed by the recited genus of polynucleotides and  $\beta$ -amyrin synthase genes. Given the lack of description of a representative number of polynucleotides, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

**[12]** Claim(s) 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an expression vector comprising a polynucleotide encoding the polypeptide of SEQ ID NO:9 and optionally further comprising the pea-derived  $\beta$ -amyrin synthase gene PSY (Morita et al., *Eur. J. Biochem.*, 267, 3543-3460, 2000) and an isolated host cell transformed with the expression vector, does not reasonably provide enablement for all expression vectors as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it

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pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

“The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue.” *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below. In view of the analysis of the Factors of *In re Wands* as set forth below, it is the examiner’s position that undue experimentation would be required for a skilled artisan to make and/or use the entire scope of the claimed invention.

The breadth of the claims: According to MPEP 2164.04, “[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims...and explicitly set forth the scope of the claim when writing an Office action.” Also, MPEP 2164.08 states, “[a]ll questions of enablement are evaluated against the claimed subject matter. The focus of the examination inquiry is whether everything within the scope of the claim is enabled. Accordingly, the first analytical step requires that the examiner

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determine exactly what subject matter is encompassed by the claims...claims are to be given their broadest reasonable interpretation that is consistent with the specification."

As noted above, the claims recite an expression vectors having a polynucleotide which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8 under a stringent condition and also encodes a polypeptide that has the activity of hydroxylating the 24-position of an oleanane type triterpene, optionally further having a  $\beta$ -amyrin synthase gene. Regarding the phrase "a polynucleotide which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8", it is noted that: 1) "a complementary chain" has been interpreted as encompassing fragments of "the polynucleotide represented by SEQ ID NO:8" of as few as two contiguous nucleotides and 2) as noted above, the phrase "polynucleotide represented by SEQ ID NO:8" has been broadly but reasonably interpreted as meaning SEQ ID NO:8 is an example of such a polynucleotide. The phrase "the activity of hydroxylating the 24-position of an oleanane-type triterpene" has been interpreted as encompassing hydroxylating position 24 of any triterpene considered to be an "oleanene-type" triterpene. Also, regarding the phrase, " $\beta$ -amyrin synthase gene", it is noted that the phrase has been interpreted as meaning any nucleic acid that encodes a polypeptide having  $\beta$ -amyrin synthase activity and although the phrase recites "gene", the phrase has not been interpreted as being limited to those nucleic acids that are "naturally-occurring". Furthermore, according to the specification at p. 13, paragraph 13, "As examples of the host, a microorganism, a plant, an animal and the like can be cited,

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though not particularly limited". As such, the transformant of claims 3 and 8 encompasses an animal, *e.g.*, a human, as the recited "host".

The broad scope of recited expression vectors is not commensurate with the enablement provided by the disclosure, particularly with regard to the scope of polynucleotides that encode a polypeptide that "has the activity of hydroxylating the 24-position of an oleanane type triterpene and  $\beta$ -amyrin synthase genes as broadly encompassed by the claims. In this case the disclosure is limited to an expression vector comprising a polynucleotide encoding the polypeptide of SEQ ID NO:9 and optionally further comprising the pea-derived  $\beta$ -amyrin synthase gene PSY (Morita et al., *Eur. J. Biochem.*, 267, 3543-3460, 2000) and an isolated host cell transformed with the expression vector.

The amount of direction provided by the inventor and The existence of working examples: The specification provides only a single working example of the recited expression vector, *i.e.*, an expression vector comprising a polynucleotide encoding the polypeptide of SEQ ID NO:9, which encodes a polypeptide that hydroxylates position 24 of  $\beta$ -amyrin and sophoradiol and optionally further comprising the pea-derived  $\beta$ -amyrin synthase gene PSY (Morita et al., *Eur. J. Biochem.*, 267, 3543-3460, 2000). This single working example fails to provide the necessary guidance for making and/or using the entire scope of recited expression vectors. For example, the specification fails to provide specific guidance regarding those nucleotides of SEQ ID NO:8 that may be altered by substitution, addition, insertion, and/or deletion with an expectation of encoding a polypeptide that maintains the desired activity of "hydroxylating the 24-

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position of an oleanane type triterpene” or those nucleotides of the pea-derived  $\beta$ -amyrin synthase gene PSY (Morita et al., *Eur. J. Biochem.*, 267, 3543-3460, 2000) that may be altered by substitution, addition, insertion, and/or deletion with an expectation of encoding a polypeptide that maintains the desired activity of  $\beta$ -amyrin synthase.

Also, regarding the scope of transformants of claims 3 and 8, the specification fails to provide guidance for generating transgenic animals, including transgenic humans, transformed with the recited expression vector. In this case, the specification fails to provide even a single working example of the claimed method being practiced in a host organism. While there is no requirement that the specification disclose a working example of the claimed invention, MPEP 2164.02 makes clear that “[l]ack of a working example, however, is a factor to be considered, especially in a case involving an unpredictable and undeveloped art.” As evidenced by the cited references (see below), gene transfer was clearly an unpredictable and underdeveloped art at the time of the invention. Further, the specification fails to provide any specific guidance that would provide the skilled artisan with an expectation of successfully practicing the claimed method in a host organism, e.g., vector used for gene transfer and method of gene transfer.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The amino acid sequence of a polypeptide determines its structural and functional properties. Predictability of which changes can be tolerated in a protein's amino acid sequence – conservative or non-conservative amino acid changes – and obtain the desired activity requires a knowledge of and guidance with regard to

which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e., expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g., multiple substitutions.

The state of the art provides evidence for the high degree of unpredictability in altering a polynucleotide sequence with an expectation that the encoded polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York, 1991) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ..they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are currently exemplified by the reference of Witkowski et al. (*Biochemistry* 38:11643-11650, 1999), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see e.g., Table 1, page 11647). Even conservative substitutions can have unpredictable effects on the function of a polypeptide. According to MPEP

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2144.08.II.A.4.(c), “[t]he effect of a conservative substitution on protein function depends on the nature of the substitution and its location in the chain. Although at some locations a conservative substitution may be benign, in some proteins only one amino acid is allowed at a given position. For example, the gain or loss of even one methyl group can destabilize the structure if close packing is required in the interior of domains. James Darnell et al., *Molecular Cell Biology* 51 (2d ed. 1990).”

Also, regarding the scope of transformants of claims 3 and 8, at the time of the invention, the ability to achieve successful gene transfer in a host organism was highly unpredictable as evidenced by the references of Dang et al. (*Clin Cancer Res* 5:471-474) and Fox (*Nat Biotechnol* 21:217). Even after the time of the invention, the art still recognizes the high level of unpredictability associated with gene transfer as evidenced by Juengst (*BMJ* 326:1410-1411).

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of a polynucleotide were known in the art at the time of the invention, it was not routine in the art to screen – by a purely trial and error process – for all polynucleotide variants having a substantial number of modifications as encompassed by the claims for those that encode polypeptides having a desired activity/utility. Regarding the scope of transformants of claims 3 and 8, since gene therapy was highly unpredictable and often unsuccessful, it is the examiner’s position that undue experimentation would be required to make *all* transformants as broadly encompassed by the claims.



In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of required experimentation, it is the examiner's position that undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

**[13]** Claim(s) 11 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to be drawn to a novel yeast strain. Since the strain is essential to the claimed invention, it must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The method for obtaining the mutant yeast strain is not fully disclosed. The enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the strain. The

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specification does not disclose a repeatable process to obtain the strain and it is not apparent if the strain is readily available to the public. Accordingly, it is deemed that a deposit of these plasmids should have been made in accordance with 37 CFR 1.801-1.809.

It is noted that applicant appears to have deposited the organism but there is no indication in the specification as to public availability. If the deposit was made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be irrevocably and without restriction or condition released to the public upon the issuance of the patent, would satisfy the deposit requirement made herein.

If the deposit has not been made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application , access to the invention will be afforded to the Commissioner upon request;
  2. all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;
  3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;
- and

4. the deposit will be replaced if it should ever become inviable.

### ***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

**[14]** Claim(s) 1-3 are rejected under 35 U.S.C. 102(b) as being anticipated by Steele et al. (*Arch. Biochem. Biophys.* 367:146-150, 1999; cited in the IDS filed on 8/25/06; “Steele”) as evidenced by Shibuya et al. (*FEBS J.* 273:948-959, 2006; “Shibuya”). See MPEP 2131.01 regarding a multiple reference 35 U.S.C. 102 rejection.

Claim 1 is drawn to an expression vector having a polynucleotide which hybridizes with a complementary chain of the polynucleotide represented by SEQ ID NO:8 under a stringent condition and also encodes a polypeptide that has the activity of hydroxylating the 24-position of an oleanane type triterpene. Claim 2 is drawn to the expression vector described in claim 1, wherein the polynucleotide is the polynucleotide represented by SEQ ID NO:8. Claim 3 is drawn to a transformant in which a host is transformed with the expression vector described in claim 1.

The reference of Steele teaches an insect cell comprising a baculovirus expression vector with a nucleic acid comprising a *CYP93E1* gene (p. 147, column 1,

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bottom), wherein the *CYP93E1* gene of Steele is 99.7% identical and 99.8% similar to SEQ ID NO:8 herein (see Appendix A sequence alignment). The reference of Shibuya is cited in accordance with MPEP 2131.01 and MPEP 2124 as showing that the polypeptide encoded by the *CYP93E1* gene of Steele encodes a polypeptide that hydroxylates position 24 of  $\beta$ -amyrin (p. 951, column 2, bottom).

This anticipates claims 1-3 as written.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

**[15]** Claim(s) 4-5 are rejected under 35 U.S.C. 103 (a) as being unpatentable over Steele (*supra*) in view of La Rosa et al. (US Patent Application Publication 2004/0031072 A1; February 2004) and Schopfer et al. (*FEBS Lett.* 432:182-186, 1998; "Schopfer"). Claims 4 and 5 limit the host to a microorganism or a yeast, respectively.

The relevant teachings of Steele are set forth above. Steele does not teach a microorganism or a yeast as an expression host.

La Rosa suggests recombinant expression in *E. coli* of a polynucleotide, SEQ ID NO:100510, that is 99.7% identical and 99.8% similar to SEQ ID NO:8 herein (see

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Appendix B sequence alignment). See La Rosa, p. 7, paragraph 66 and 68 and p. 13, claim 1.

Schopfer teaches recombinant expression of a soybean cytochrome P450-dependent enzyme in a yeast host cell optimized for expression of cytochrome P450 enzymes (p. 182, abstract and p. 183, column 2, bottom).

Therefore, it would have been obvious to one of ordinary skill in the art to combine the teachings of Steele, La Rosa, and Schopfer to transform an *E. coli* or yeast host cell with an appropriate expression vector comprising the polynucleotide of Steele. One would have been motivated to do this because of the express teachings of La Rosa or because the yeast of Schopfer is optimized for cytochrome P450 recombinant protein expression. One would have a reasonable expectation of success to transform an *E. coli* or yeast host cell with an appropriate expression vector comprising the polynucleotide of Steele because of the results of Steele, La Rosa, and Schopfer. Therefore, claims 4-5, drawn to the transformant as described above would have been obvious to one of ordinary skill in the art.

### **Conclusion**

**[16]** Status of the claims:

Claims 1-16 are pending.

Claims 12-16 are withdrawn from consideration

Claims 1-11 are rejected.

No claim is in condition for allowance.

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Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/David J. Steadman/  
David J. Steadman, Ph.D.  
Primary Examiner  
Art Unit 1656

## APPENDIX A

AF135485  
LOCUS AF135485 1850 bp mRNA linear PLN 02-AUG-1999  
DEFINITION Glycine max cytochrome P450 monooxygenaseCYP93D1 (CYP93E1) mRNA, complete cds.  
ACCESSION AF135485  
VERSION AF135485.1 GI:5059125  
KEYWORDS .  
SOURCE Glycine max (soybean)  
ORGANISM Glycine max  
Eukaryota; Viridiplantae; Streptophyta; Embryophyta; Tracheophyta; Spermatophyta; Magnoliophyta; eudicotyledons; core eudicotyledons; rosids; eurosids I; Fabales; Fabaceae; Papilionoideae; Phaseoleae; Glycine.  
REFERENCE 1 (bases 1 to 1850)  
AUTHORS Steele,C.L., Gijzen,M., Qutob,D. and Dixon,R.A.  
TITLE Molecular characterization of the enzyme catalyzing the aryl migration reaction of isoflavonoid biosynthesis in soybean  
JOURNAL Arch. Biochem. Biophys. 367 (1), 146-150 (1999)  
PUBMED 10375412  
REFERENCE 2 (bases 1 to 1850)  
AUTHORS Steele,C.L., Gijzen,M., Qutob,D. and Dixon,R.A.  
TITLE Direct Submission  
JOURNAL Submitted (17-MAR-1999) Plant Biology, Noble Foundation, 2510 Sam Noble Pkwy, Ardmore, OK 73402, USA  
FEATURES Location/Qualifiers  
source 1. .1850  
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CDS 55. .1596  
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/db\_xref="GI:5059126"  
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## ORIGIN

Query Match 99.7%; Score 1537.2; DB 4; Length 1850;  
Best Local Similarity 99.8%; Pred. No. 0;  
Matches 1539; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

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 Qy 61 ATACGTTCCATCTTCAAGAAACCACAGCGTCTAAGACTCCCACGGGTCCTCCAATTTC 120  
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 Db 115 ATACGTTCCATCTTCAAGAAACCACAGCGTCTAAGACTCCCACGGGTCCTCCAATTTC 174  
 Qy 121 GTACCCTTGCTGGGACACGCGCCATATCTCCGTTCACTGCTCCACCAAGCCTTGTACAAG 180  
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 Db 175 ATACCCTTGCTGGGACACGCGCCATATCTCCGTTCACTGCTCCACCAAGCATTGTACAAG 234

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Db	475	AAGACCCCTGGAGCATTTTCGTGAGAATCCGCGAGAGCGAGGTGGAGGCGTTCTCAAGAGA	534
Qy	481	ATGATGGAGATTTTCAGGCAATGGAAATTACGAGGTGGTGATGAGGAAGGAGCTCATAACG	540
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Db	595	CACACGAATAACATCATCACGAGGATGATAATGGGGAAGAAGAGTAATGCGGAAAACGAT	654
Qy	601	GAGGTGGCCAGGTTGAGGAAGGTGGTGAGGGAGGTCGGGGAGTTGCTTGGGGCGTTTAAC	660
Db	655	GAGGTGGCCAGGTTGAGGAAGGTGGTGAGGGAGGTCGGGGAGTTGCTTGGGGCGTTTAAC	714
Qy	661	TTGGGGGATGTTATTGGGTTTCATGAGGCCTTTGGATCTGCAAGGGTTTGGGAAGAAGAAC	720
Db	715	TTGGGGGATGTTATTGGGTTTCATGAGGCCTTTGGATCTGCAAGGGTTTGGGAAGAAGAAC	774
Qy	721	ATGGAAACTCACCACAAGGTGGATGCGATGATGGAGAAGGTGTTGAGGAGCATGAGGAG	780
Db	775	ATGGAAACTCACCACAAGGTGGATGCGATGATGGAGAAGGTGTTGAGGAGCATGAGGAG	834
Qy	781	GCTAGGGCTAAGGAAGATGCTGACTCTGATAGGAAGAAGGATCTTTTTGATATTTTGTG	840
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Qy	841	AACCTCATTGAAGCTGATGGTGCTGACAATAAGCTCACTAGAGAGAGTGCCAAAGCCTTT	900
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Qy	901	GCTCTGGACATGTTTCATCGCCGGCACAAACGGCCCCGCAAGCGTCCTAGAGTGGTCACTG	960
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**APPENDIX B**

US-10-424-599-100510  
; Sequence 100510, Application US/10424599  
; Publication No. US20040031072A1  
; GENERAL INFORMATION:  
; APPLICANT: La Rosa Thomas J  
; APPLICANT: Kovalic David K  
; APPLICANT: Zhou Yihua  
; APPLICANT: Cao Yongwei  
; TITLE OF INVENTION: Soy Nucleic Acid Molecules and Other Molecules Associated With  
; TITLE OF INVENTION: Plants and Uses Thereof for Plant Improvement  
; FILE REFERENCE: 38-21(53223)B  
; CURRENT APPLICATION NUMBER: US/10/424,599  
; CURRENT FILING DATE: 2003-04-28  
; NUMBER OF SEQ ID NOS: 285684  
; SEQ ID NO 100510  
; LENGTH: 2278  
; TYPE: DNA  
; ORGANISM: Glycine max  
; FEATURE:  
; NAME/KEY: unsure  
; LOCATION: (1)..(2278)  
; OTHER INFORMATION: unsure at all n locations  
; FEATURE:  
; OTHER INFORMATION: Clone ID: PAT\_MRT3847\_61775C.1  
US-10-424-599-100510

Query Match 99.7%; Score 1537.2; DB 9; Length 2278;  
Best Local Similarity 99.8%; Pred. No. 0;  
Matches 1539; Conservative 0; Mismatches 3; Indels 0; Gaps 0;

Qy 1 ATGCTAGACATCAAAGGCTACCTCGTACTCTTCTCCTATGGTTCATATCAACCATTCTG 60  
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